(HSCT). Outcomes with myelaoblative conditioning have been surprisingly poor with almost 1/3 of patients succumbing to early transplant related mortality (TRM). Most of the fatalities occur due to cardiopulmonary failure. Mortality is higher than that in other immunodeficiency syndromes, however the reasons for this increased toxicity are unclear.
We hypothesized that prolonged steroid exposure during HLH therapy may cause the development of cardiac hypertrophy. Compromised cardiac reserve could contribute to poor outcome because of the multiple physiological stressors associated with transplant.
We reviewed the records of 11 consecutive children undergoing HSCT at our institution from January 2004- December 2012. The age at diagnosis ranged from birth to 60 (median 2.5) months and the age at HSCT from 6-70 (median 9) months. 8/11 had identified genetic defects (5 perforin, 2 MUNC, 1 Griscelli). All 11 received pre-HSCT therapy with etoposide, cyclosporin and dexamethasone. 10/11 were in complete disease remission at the time of HSCT. Conditioning was fully ablative in 9/11(Bu, Cy, VP, ATG) and reduced intensity in 2 (Flu/campath). 6 received marrow as stem cell source. Donors were matched sibling in 1, and unrelated donor in 5. 5 received unrelated umbilical cord. All patients except the sibling donor received methylprednisonole at 1-2 mg/kg/day as GVHD prophylaxis. 3 had acute GVHD and received additional therapy with high dose (>2 mg/kg/day) steroids.
Pre transplantation echocardiograms were accessible for 6 patients; none had evidence of LVH. Post transplantation echocardiograms were reviewed for all patients. 7/11 (64%) never evidenced LVH at any point post-HSCT. TRM in this group was 3/7 (42%) due to multi-organ system failure (MOSF) (2) and adenovirus infection (1). 4/11 patients (36%) developed LVH 1 - 18 weeks post-HSCT. TRM was 100% in this group, higher than those without LVH (p=0.58) and all due to MOSF. Infectious agents were only identified in $^{1}/_{4}$ (adeno / EBV) and recurrent HLH in one.
In light of these findings, particular attention to cardiac status in patients with HLH is highly recommended. Further investigation is needed to identify pre and post SCT factors contributing to cardiac hypertrophy. This will allow both preventative measures to be developed and optimal management to be provided when these patients become critically ill.

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Outcome after Allogeneic Stem Cell Transplant for Patients with Hematological Malignancies and Associated Chromosome 7 Deletions

Swati Naik [1], Fatma Okur [2], Bilal Omer [2], Pulivarthi Rao [3], Caridad Martinez [1], Kathryn Leung [1], Jesse Wu [1], Nabil Ahmed [1], Carl Allen [1], Stephen Gottschalk [4], Helen E. Heslop [5], Malcolm K. Brenner [6], Robert A. Krance [6]. [1] Center for Cell and Gene Therapy, Baylor College of Medicine, Texas Children's Hospital, Houston, TX; [2] Center for Cell and Gene Therapy, Baylor College of Medicine, Houston, TX; [3] Pediatric Hematology/Oncology, Texas Children's Hospital, Houston, TX; [4] Center for Cell and Gene Therapy, Dept. of Pediatrics, Baylor College of Medicine, Houston Methodist Hospital and Texas Children's Hospital, Houston, TX; [5] Center for Cell and Gene Therapy, Dept. of Pediatrics, Dept. of Medicine, Baylor College of Medicine, Houston Methodist Hospital and Texas Children's Hospital, Houston, TX; [6] Center for Cell and Gene Therapy, Baylor College of Medicine, Texas Children's Hospital, The Methodist Hospital, Houston, TX

Chromosome 7 deletions are adverse prognostic factors associated with worse outcomes in patients with hematological malignancies. However there are few outcome data for hematopoietic stem cell transplant (HSCT) in pediatric patients with hematological malignancies and chromosome 7 deletions. We now describe the outcome in 40 patients with chromosome 7 abnormalities (ALL, n=13, AML, n=11, MDS, n=14 and JMML, n=2) who received an allogeneic HSCT at our institution between 2001-2013. The median age at the time of transplant was 9 years (range: 1-18 years). There were 23 patients with monosomy 7, 12 with 7q- and 5 with 7p-. At the time of transplant, 16 of the 24 patients with acute leukemia (ALL/AML) were in CR (9-CR1, 6-CR-2, 1-CR3) and 8/24 had active disease (3 with primary refractory disease, 5 in relapse). All patients with ALL (13/13), 10/11 patients with AML and 1 /2 patients with JMML received chemotherapy prior to transplant, while patients with MDS received no prior therapy. Patients received HSCT from MRD (10), MUD (17), MMUD (4) or haploidentical donors (9). The median time to engraftment was 19 days (95%CI: 17-20 days). With a median follow up of 857 days (range 5 -4099 days), the 3-year overall survival (OS) and disease free survival (DFS) for the entire cohort was 60% and 53%, respectively. The OS and DFS correlated with the underlying diagnosis with MDS patients having better 3-year OS and DFS (OS: MDS (77%), AML (36%), ALL (67%), JMML (50%) and DFS: MDS (64%), AML (36%), ALL (58%), JMML (50%) Outcome was not significantly affected by the type of chromosome 7 deletion (3-year OS: monosomy 7 (59%), 7q- (53%), 7p- (80%), $p = 0.528$). Upon further subdivision by diagnosis, patients with MDS that had associated monosomy 7 had significantly better OS compared to patients with AML and monosomy 7 as well as ALL and monosomy 7 ($p = 0.014$ and $p = 0.029$, respectively). Patients with MDS and associated chromosome 7 deletions, in particular monosomy 7, may achieve very good OS and DFS after HSCT. In contrast, patients with AML do not fare as well after HSCT.

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Outcome after Stem Cell Transplant in Patients with Dyskeratosis Congenita

Swati Naik [1], Ghadir Sasa [1], Alison Bertuch [2], Caridad Martinez [1], Bilal Omer [3], Carl Allen [1], Nabil Ahmed [1], Stephen Gottschalk [4], Helen E. Heslop [5], Malcolm K. Brenner [6], Robert A. Krance [6], Kathryn Leung [1]. [1] Center for Cell and Gene Therapy, Baylor College of Medicine, Texas Children's Hospital, Houston, TX; [2] Pediatrics, Baylor College of Medicine, Houston, TX; [3] Center for Cell and Gene Therapy, Baylor College of Medicine, Houston, TX; [4] Center for Cell and Gene Therapy, Dept. of Pediatrics, Baylor College of Medicine, Houston Methodist Hospital and Texas Children's Hospital, Houston, TX; [5] Center for Cell and Gene Therapy, Dept. of Pediatrics, Dept. of Medicine, Baylor College of Medicine, Houston Methodist Hospital and Texas Children's Hospital, Houston, TX; [6] Center for Cell and Gene Therapy, Baylor College of Medicine, Texas Children's Hospital, The Methodist Hospital, Houston, TX

Dyskeratosis congenita is a rare inherited bone marrow failure and cancer predisposition syndrome with multisystem involvement. While allogeneic hematopoietic stem cell transplant (HSCT) can cure the bone marrow failure, reported survival is low, with patients suffering unusual complications post HSCT. We describe the long term outcome in 6 patients with mutation proven DC following an allo-HSCT at our institution between 1997–2011. To our knowledge this is the first report to begin to correlate genotype to phenotype post HSCT. The median age was 4 years (range: 2–13). 4 patients had mutations in the *TINF2* gene, 1 in *DKC1* and 1 had a homozygous *TERT* mutation. 4/6 patients received reduced intensity conditioning (RIC) regimens and

Age (yrs)	Sex	Mutation	Complications post HSCT	Survival
5	F	*TINF2*	Pulmonary: Pulmonary fibrosis Renal: Hemolytic uremic syndrome, CKD Vascular: Venous malformations Heme: Hypocellular marrow Other DC related: Leukoplakia, nail dystrophy, alopecia, lacrimal duct stenosis, vaginal stenosis, osteoporosis, femur fracture	Alive
4	F	*TINF2*	Pulmonary: Pulmonary fibrosis GI: Massive GI bleeding, ascites Renal: Hepatorenal syndrome Heme/BMT: Hypocellular marrow Other DC related: Lacrimal duct stenosis	Dead
5	M	*TINF2*	GI: Massive GI bleeding, ascites Heme/BMT: Hypocellular marrow, oral GVHD ID: Disseminated adenovirus	Alive
2	M	*TINF2*	GI: Massive GI bleeding, intestinal obstruction and perforation Renal: Thrombotic microangiopathy, AKI Heme/BMT: Acute GVHD (gut, liver,skin) Other DC related: Urethral meatus stenosis ID: HHV6, C difficile colitis	Dead
13	M	*DKC1*	GI: Esophageal stricture	Alive
3	M	*TERT*	Heme/BMT: Acute gut GVHD	Alive

2 received myeloablative conditioning regimens (MAC). Patients received HSCT from MRDs (4) and MMUDs (2). 5/6 patients engrafted with the 1st HSCT. One patient had primary engraftment failure and was rescued with a 2nd HSCT from the same donor using MAC. 3/6 six patients developed GVHD (acute GVHD – 2, chronic extensive GVHD -1). 4/6 patients are alive (OS: 67%) with a median follow up of 1753 days (range: 92–5963). However, all 4 patients with *TINF2* mutations suffered unusual multi-system complications which developed late (4–5 years) after HSCT. The 2 patients with *DKC1* and *TERT* mutation had no such atypical complications and are doing well at last follow up. Recent reports describe a more severe phenotype in patients with *TINF2* mutations and the extra-hematopoietic manifestations that continue after transplantation suggest that HSCT can have only limited impact on the natural course of their disease and on their long-term outcome. These patients require close multi-disciplinary follow up after HSCT to ensure early detection of complications. Future improvements could focus on the use of less toxic RIC regimens, measurement of biomarkers to predict complications and perhaps novel therapies to correct the underlying telomere defect.

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HLA Identical Siblings Are the Best Donors for Children with ALL

Christina Peters [1], Andre Schrauder [2], Martin Schrappe [2], Arend von Stackelberg [3], Peter Bader [4], Wolfram Ebell [5], Peter Lang [6], Bernhard Kremens [7], Karl-Walter Sykora [8], Ingo Mueller [9], Karoline Ehlert [10], Michael Albert [11], Wolfgang Holter [12], Brigitte Strahm [13], Susanne Matthes-Martin [14], Roland Meisel [15], Tayfun Gungor [16], Bernd Gruhn [17], Ansgar Schulz [18], Wilhelm Woessmann [19], Martin Zimmermann [20], Ulrike Poetschger [21], Thomas E. Klingebiel [4]. [1] Stem Cell Transplantation Unit, St. Anna Children's Hospital, Vienna, Austria; [2] Department of Paediatrics, University Hospital Schleswig-Holstein, Kiel, Germany; [3] Charité, Berlin, Germany; [4] Stem Cell Transplantation and Immunology, Klinik für Kinder und Jugendmedizin, Frankfurt am Main, Germany; [5] Pediatric BMT Unit, University Hospital Charite-Virchow, Berlin, Germany; [6] Hematology / Oncology, University Children's Hospital Tuebingen, Tuebingen, Germany; [7] University Hospital, Essen, Germany; [8] University Hospital, Hannover, Germany; [9] Department of Pediatrics, Universitats-Kinderlinik Hamburg, Hamburg, Germany; [10] Pediatric Hematology and Oncology, University Children's Hospital, Muenster, Germany; [11] Pediatric Hematology/Oncology, Dr. von Haunersches Kinderspital, Muenchen, Germany; [12] St. Anna Children's Hospital, Wien, Austria; [13] University Hospital, Freiburg, Germany; [14] BMT Unit, St. Anna Children's Hospital, Vienna, Austria; [15] University Hospital, Duesseldorf, Germany; [16] University Childrens Hospital, Zurich, Switzerland; [17] Department of Pediatrics, Jena University Hospital, Jena, Germany; [18] Universitatsklinikum Ulm Klinik fur Kinder, Ulm, Germany; [19] Department of Pediatric Hematology and Oncology, Justus Liebig University, Giessen, Germany; [20] Hannover Medical School, Hannover, Germany; [21] St. Anna Children's Cancer Research Institute, Wien, Austria

Allogeneic hematopoietic stem cell transplantation (HSCT) from unrelated donors became a common practice during the last years to rescue children and adolescents with high risk acute lymphoblastic leukaemia (ALL) who lack an HLA identical sibling donor (MSD). However, heterogeneous approaches in donor selection and transplantation methods hamper the interpretation of available data. Therefore we compared the influence of donor source under standardized methods. Twenty-nine centres participated in the prospective trial to evaluate whether the results of HSCT from HLA matched donors (MD) are comparable to those of HLA identical siblings in patients with high risk ALL.

118 patients (age 0.5-18 years, med. 10.2) underwent MSD-HSCT and 313 MD-HSCT. 218 pts were in first and 213 beyond 1st remission. Unrelated donors were compatible for at least 9/10 matches with allelic typing. GvHD-prophylaxis consisted of CSA only after MSD-HSCT and of CSA/MTX/ATG after MD-HSCT. Patients older than 2 years received total body irradiation and etoposide as conditioning regimen. The stem cell source was for 82% of the MSD-group bone marrow (BM), 10% received peripheral blood stem cells (PBSC) and some received cord blood (CB). In the MD-cohort, 66% received BM, 28% PBSC and the remaining CB or combinations.

Results: After a median follow up of 4.2 years, the 4-year disease free survival (DFS) is 0.70±0.04, the overall survival (OS) 0.77±0.04 after MSD-HSCT and after MD-HSCT DFS is 0.66±0.03, OS 0.73±0.03 (n.s.); 4-years relapse-incidence is 0.22±0.04 after MSD-HSCT and 0.23±0.02 after MD-HSCT (n.s.). Non-relapse mortality at 4 years is 0.06±0.02 for MSD and 0.10±0.02 for MD (p-value 0.228). In multivariate analysis the only significant impact on OS and DFS was 1st remission compared to 2nd or 3rd remission with a Hazard ratio of 1.71. However, engraftment was significantly better after MSD-HSCT: the median day to reach ANC >1000/µl/lymphocytes >100/µl/platelets >50.000/µl was 17/14/22 after MSD-HSCT and 22/23/32 after MD-HSCT ($p < 0.001$). This resulted in significant less severe infections (≥ grade 3 CTA 3.0) –18% vs. 40% ($p < 0.01$) and less severe pulmonary complications: 10% vs. 19% ($p = 0.034$).